

REMARKS

At the outset, Applicants wish to thank Examiners Counts and Le for the telephone interview conducted by Applicant's representatives Mark FitzGerald and Barbara Gyure on February 11, 2005. During the interview, all pending claims were discussed, with particular emphasis on independent claims 1 and 51. More particularly, the rejection under 35 U.S.C. §112, second paragraph regarding the detection of positive signal from the detector molecule regardless of binding between the tagged binding partner polypeptide and the binding partner polypeptide was discussed. The Examiner agreed that the specification provides support for assays in which a detector molecule that may give a signal even when the binding partners are unbound would work to provide a meaningful result. The Examiner agreed to consider the clarifying amendments proposed herein.

Claims 1-5, 7-13, 27, 28, 30, 32-34, 51 and 52 are currently under examination in the application. Claims 35-50 and 55-80 are withdrawn. Claims 1 and 51 are proposed to be amended. The amendments find support in the specification and are discussed in the relevant sections below. No new matter is added.

Claim Objection:

The Office Action objects to Claim 1, stating that the recitation in part (B) "of a said tagged binding partner polypeptide" should be "of said tagged binding partner polypeptides." Applicants have amended the language herein to recite "of said one or more tagged binding partner polypeptides." Support for the language of the amendment is found, for example, at page 9, lines 7-9. Applicants submit that the proposed amendment is sufficient to overcome the objection and respectfully request that it be withdrawn.

Rejection under 35 U.S.C. §112, Second Paragraph:

The Office Action rejects claims 1-5, 7-13, 27, 28, 30, 32-34, 51 and 52 as vague and indefinite under 35 U.S.C. §112, second paragraph, stating

"The detector molecule as recited binds to the tagged binding partner and regardless if the tagged binding partner binds to the binding partner polypeptide or not the detector molecule will bind to the tagged binding partner and thus a

positive signal will always be detected. Claims 1 and 51 as instantly recited will not work.”

As discussed in the interview, Applicants submit that the specification recites a number of assay formats in which a meaningful result can be obtained using a detector molecule as recited, even where the detector molecule may have a detectable signal when the binding partners are not bound to each other. The possibility that the recited detector molecule may give a detectable signal when associated with the tag of the tagged binding partner polypeptide independent of the binding of the tagged binding partner to a binding partner polypeptide is not relevant where the binding is evidenced by a *change* in a signal generated by the reporter molecule.

For example, the specification describes the use of Fluorescence Correlation Spectroscopy (FCS) at page 75, line 3 to page 76, line 2. As noted in the specification, FCS measures the motion of diffusion of a tagged molecule. The specification states:

In FCS, a focused laser beam illuminates a very small volume of solution, on the order of 10-15 liter, which at any given point in time contains only one molecule of the many under analysis. The diffusion of single molecules through the illuminated volume, over time, results in bursts of fluorescent light as the labels of the molecules are excited by the laser. Each individual burst, resulting from a single molecule, can be registered.

A labeled polypeptide will diffuse at a slower rate if it is large than if it is small. Thus, multimerized polypeptides will display slow diffusion rates, resulting in a lower number of fluorescent bursts in any given time frame, while labeled polypeptides which are not multimerized or which have dissociated from a multimer will diffuse more rapidly. Binding of polypeptides according to the invention can be calculated directly from the diffusion rates through the illuminated volume. (page 75, lines 9-19; emphasis added)

Thus, even where the fluorescent tag gives a detectable signal independent of the binding status of the binding partners under investigation, when FCS is used for detection, that signal will *change* or be altered in a manner that is dependent upon the binding status of the partners.

As another example, assays in which FRET is used to detect binding (described in the specification at numerous places, e.g., page 9, line 19 to page 10, line 2, page 21, line 17 to page 22, line 3, to name but two) are functional in the instance where one or both members of the fluorescent donor/acceptor pair are detectable regardless of binding status. Here again, the

detected signal *changes* in a manner dependent upon the binding status of the binding partner polypeptides.

As another example, the specification describes the use of Fluorescence Polarization (FP), which measures changes in the rotation of a fluorescently tagged molecule. The specification states at page 76, line 11 to page 77, line 2:

Fluorescently labeled binding partner polypeptides emit light in the same polarized plane when excited with plane polarized light if the molecule remains stationary throughout the excited state. However, the excited molecule can rotate or tumble out of the plane of polarized light during the excited state and emit light in a different plane. Emission light intensity can be monitored in more than one plane. *The degree to which emission intensity moves from one plane to another plane is related to the mobility of the fluorescently labeled binding partner polypeptide. Where a fluorescently labeled binding partner polypeptide is bound to its corresponding binding partner, it will move very little during the excited state interval because it is a large molecule, and the emitted light will remain highly polarized with respect to the excitation plane. If a fluorescently labeled binding partner is not bound to its corresponding binding partner it will rotate or tumble faster because it is a small molecule. The resulting emitted light will be depolarized relative to the excitation plane.* (Emphasis added)

Thus, when using FP for detection, even though a detector molecule may give a signal when binding partner polypeptides are bound or unbound, the change in the size of the complex upon binding will yield a *change* in the signal detected. Applicants submit that the same is true when, for example, fluorescence anisotropy, which also measures the rotation of fluorescent molecules (see page 76, lines 3-8), is used.

In view of the above, Applicants submit that the invention as claimed in independent claims 1 and 51 will work. As discussed during the interview, and simply to remove any doubt, Applicants propose herein to amend each of claims 1 and 51 to recite “wherein said binding is evidenced by a change in a signal generated by said reporter molecule.” Applicants note that such a change includes, for example, a change in the diffusion rate of a labeled molecule or complex, a change in the rotational rate of a labeled molecule or complex, a change in emission spectrum of a fluorescent label, as well as, for example, a change in the location of signal from a label, e.g., when a labeled molecule in solution binds to an immobilized binding partner. In view of the above and the proposed amendment, Applicants submit that the invention as claimed in the

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amended claims will work, and respectfully request that the rejection under §112, second paragraph be withdrawn.

Applicants also wish to point out one additional amendment proposed to clarify that which is claimed. In claim 51, part (B), Applicants propose to remove the language “that are not substrates of said one or more enzymes.” Applicants submit that this language was mistakenly included as an amendment in the “Listing of the Claims” provided in the Office Action response filed October 26, 2004. The Examiner will note that the language was not discussed in the “Remarks” section of that response, and that the claim as proposed to be amended herein (i.e., without that language) remains novel and non-obvious over the cited references, in part due to the failing of each of the cited references to teach or suggest a detector molecule that “associates with a tag of said tagged binding partner polypeptides” as required by the claim. The amendment adds no new matter.

In view of the above, Applicants submit that all issues raised in the Final Office Action have been addressed herein. Applicants respectfully request entry of the amendments and reconsideration of the claims.

Respectfully submitted,

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